EFFICACY REVIEW

Product(s): Bromethalin Bait, Purina Assault Rat Pellets, Purina Assault Rat Place Pack, Purina Assault Rat Place Pack II, and Hot Shot Sudden Death™ Brand Rat Killer 1

Date: January 29, 2004

EPA Reg No(s): 67517-63, 67517-73, 67517-74, 67517-75, and 8845-126

DP Bar code(s): D287914, D287915, D287916, D287917, and D287918

Chemical Code: Bromethalin 112802

Formulation(s): Bromethalin Baits (Pellets)

Purpose for Review: The purpose for this review is to determine if the previously submitted efficacy tests dated June 21, 1990, November 24, 1992, and August 24, 1995, are acceptable for reregistration of the above named products.

MRID No(s):

41591202C Dickerson, C. W. June 21, 1990. Contains 0.01% Bromethalin Purina Last : N-Methyl 1-2, 4-Dinitro-N-(2, 4, 6-Tribromophenyl)-6-(Trifluoromethyl) Benzenamine. Purina Mills, Inc. Unpublished Report. Experiment #760. 44pp.

41591203C Dickerson, C. W. June 21, 1990. Contains 0.01% Bromethalin Purina Last : N-Methyl 1-2, 4-Dinitro-N-(2, 4, 6-Tribromophenyl)-6-(Trifluoromethyl) Benzenamine. Purina Mills, Inc. Unpublished Report. Experiment #761. 44pp.

43689201C Dickerson, C. W. November 24, 1992. Efficacy Testing of a Pelleted Rodenticide Bait Packaged in Place Packs. PM Resources, Inc. Unpublished Report. Experiment #893. 65pp.

43859001C Dickerson, C. W. August 24, 1995. Efficacy testing of a pelleted rodenticide bait, packaged in place packs and offered to laboratory rats. Vol 1. PM Resources, Inc. Unpublished Report. Experiment. 41pp. #971.

43859002C Dickerson, C. W. August 24, 1995. Efficacy testing of a pelleted rodenticide bait, packaged in place packs and offered to laboratory rats. Vol 2. PM Resources, Inc. Unpublished Report. Experiment. 41pp. #972.

43859003C Dickerson, C. W. August 24, 1995. Efficacy testing of a pelleted rodenticide bait, packaged in place packs and offered to laboratory rats. Vol 3. PM Resources, Inc. Unpublished Report. Experiment. 41pp. #973.

42025103C Dickerson, C. W. June 21, 1990. Contains 0.01% Bromethalin Purina Last : N-Methyl 1-2, 4-Dinitro-N-(2, 4, 6-Tribromophenyl)-6-(Trifluoromethyl) Benzenamine. Purina Mills, Inc. Unpublished Report. Experiment. 43pp. #761.

42025102C Dickerson, C. W. June 21, 1990. Contains 0.01% Bromethalin Purina Last : N-Methyl 1-2, 4-Dinitro-N-(2, 4, 6-Tribromophenyl)-6-(Trifluoromethyl) Benzenamine. Purina Mills, Inc. Unpublished Report. Experiment. 43pp. #760.

Good Laboratory Practices: Yes

Branch Chief: Meredith Laws

Team Leader: John Hebert, Product Manager 07

IRB Reviewer: Geraldine R. McCann, Environmental Protection Specialist

BACKGROUND: PM Resources has applied for reregistration of their **Bromethalin Bait** (67517-63), **Purina Assault Rat Pellets** (67517-73), **Purina Assault Rat Place Pack** (67517-74), **Purina Assault Rat Place Pack II** (67517-75), and the Spectrum Group has requested reregistration of their product: **Hot Shot Sudden Death™ Brand Rat Killer 1** (8845-126). Previous efficacy reviews for these products were conducted by William W. Jacobs and will be used to evaluate the data presented for reregistration. The efficacy data guidelines used to screen the bait for effectiveness for these products are OPP 1.209 and 1.219. This review will evaluate the results of the studies and determine if the data are still acceptable.

REVIEW OF DATA:

1. **41591202C** Dickerson, C. W. (1990) Contains 0.01% Bromethalin Purina Last : N-Methyl 1-2, 4-Dinitro-N-(2, 4, 6-Tribromophenyl)-6-(Trifluoromethyl) Benzenamine. Purina Mills, Inc. Unpublished Report. Experiment. 44pp. #760.

DISCUSSION: Efficacy reviews were conducted by W. Jacobs on May 6, 1992, April 25, 1995, May 5, 1997, and June 30, 1998. He listed one other review date (October 4, 1990) that was not located in the jacket for this product, but can be found in the jacket for 602-316 (67517-74). This product is an "acute" toxic bait offered for sale as dry 3/16" pelleted bait for control of Norway rats and roof rats. The bait made for the studies (April 6, 1990) is the same formulation currently conveyed on the CSF dated May 2, 1997. (I think this is a copying error and the date should

be May 28, 1997.) In the efficacy review by W. Jacobs (May 6, 1992), he states: "This product was registered without an efficacy review. This bait is claimed to be identical in formulation to PURINA ASSAULT RAT PLACE PACK BRAND (602-316) but is packaged in bulk ("loose bait") form and , as a result, has slightly different application directions on its label." In a later paragraph, W. Jacobs states "New efficacy data were submitted. These studies were assigned MRID Nos. 42025102 and 42025103. In her letter of 9/6/91, Kelly Kraft of Purina Mills states that these studies are copies of tests submitted previously for 602-316 and assigned MRID Nos. 41591202 and 41591203. Those studies were discussed in the efficacy review of 10/4/90 for 602-316 and were accepted. I have examined the report of efficacy studies submitted for 602-322 and have concluded that these reports refer to the same studies that were submitted earlier for 602-316 and that were cited by Ms. Kraft. No /Additional efficacy studies are required for 602-322." The protocol (OPP guideline 1.209) used in this efficacy study was written in 1974, and was updated in 1991.

The rats were wild-type captured and weighed April 30, 1990. They were weighed 7 days before the test start. The guidelines specify (1.209, 2.1) the rats should not have a maximum difference in average weights between the sexes of more than 65 g and they should not be weighed more than 3 days before the test. The rats had a maximum acceptable difference in average weights of 28.6 g one week before the testing.

Information about the cage type and size, feeders and their design, and the pretest holding conditions were not available in the study documentation (1.209, 3 and 4). The temperature, humidity and light conditions pretest, holding, and testing were not documented as well (1.209, 5.1). Information regarding the animal's water system was not explained (1.209, 6.2), and how spillage was recaptured was not discussed (1.209, 6.3) . These conditions may affect the outcome of the testing if they are extreme.

The composition and formulation of the OPP rat and mouse challenge diet (page 11 of 44 and raw data on page 20 of 44) was well documented as well as the bait formulation (page 8, raw data page 19 of 44) and analysis (pages 23 to 30 of 44). The male and female control groups were used for MRID 41591202 (test #760) and 41591203 (test #761).

This test consisted of a minimum of two groups of rats (20 each) as needed to perform this test (1.209, 6.1). Test guideline 1.209, 7.5 states " This laboratory efficacy test should be replicated at least once." One more group of 20 animals should have been included to repeat the test. In this version of the test guidelines where the "single-feeding" claim is being pursued, a container must be switched to the other side of the cage with the opposite container after 12 hours (1.209,6.4) to show no preference to cage side or test dish type. No documentation is found to show that this was done.

The test results are summarized below:

Table 1. Wild Rats on Pelleted Bromethalin Bait

Pretest Weights 1-Day Test-Consumption and Mortality

Sex	Average Group Weight (g)	OPP Diet Consumed (g)	Treated Bait Consumed (g)	Total Bait Consumption (g)
M (10)	315.2	35.8	146.1	181.9
F (10)	289.1	**100% Mortality**		Percent **Pelleted Bait** Consumed **80.3%**
Total (20)	Group Difference 26.1			

Table 2. Wild Rats on Control Bait

Pretest Weights 3-Day Test-Consumption and Mortality

Sex	Average Group Weight (g)	OPP Diet Consumed (g)	Total Bait Consumption (g)
M (10)	294.6	362.7	362.7
F (10)	238.7	**0% Mortality**	
Total (20)	Group Difference 55.9		

2. **41591203C** Dickerson, C. W. (1990) Contains 0.01% Bromethalin Purina Last : N-Methyl 1-2, 4-Dinitro-N-(2, 4, 6-Tribromophenyl)-6-(Trifluoromethyl) Benzenamine. Purina Mills, Inc. Unpublished Report. Experiment. 43pp. #761.

DISCUSSION: Previous efficacy reviews for this product were conducted by W. Jacobs on January 6, 1982; June 4, 1982; September 29, 1982; January 7, 1983; and April 2, 1997. In the efficacy review from January 6, 1982, W. Jacobs states that "The active ingredient has never before been registered as a pesticide." Bromethalin "is very toxic to target species. An early symptom of toxicosis is anorexia." In his September 29, 1982 review, he states: "Bromethalin is a new rodenticide compound. It has been thoroughly tested and found effective in this formulation against Norway rats and house mice, but not against roof rats." The product was registered October 21, 1982 (1471-121). "Roof rat claims and use directions proposed for this product..." were accepted in W. Jacobs January 7, 1983, review. In a letter drafted 9/6/91, Kelly Kraft of Purina Mills states that these studies are copies of tests submitted previously for 602-316 (67515-74) and assigned MRID Nos. 41591202 and 41591203. Those studies were discussed in the efficacy review of 10/4/90 for 602-316 (67515-74) and were accepted. The protocol (OPP guideline 1.209) used in this efficacy study was written in 1974, and was updated in 1991.

The rats were wild-type captured and weighed April 30, 1990. They were

weighed 7 days before the test start (May 7, 1990). The guidelines specify (1.209, 2.1) the rats should not have a maximum difference in average weights between the sexes of more than 65 g and they should not be weighed more than 3 days before the test. The rats had a maximum acceptable difference in average weights of 12.1 g one week before the testing.

Information about the cage type and size, feeders and their design, and the pretest holding conditions were not available in the study documentation (1.209, 3 and 4). The temperature, humidity and light conditions pretest, holding, and testing were not documented as well (1.209, 5.1). Information regarding the animal's water system was not explained (1.209, 6.2), and how spillage was recaptured was not discussed (1.209, 6.3) . These conditions may affect the outcome of the testing if they are extreme.

The composition and formulation of the OPP rat and mouse challenge diet (page 11 of 43 and raw data on page 38 of 43) was well documented as well as the bait formulation (page 10, raw data page 37 of 43) and analysis (pages 23 to 30 of 43). The male and female control groups were used for MRID 41591202 (test #760) and 41591203 (test #761).

This test consisted of a minimum of two groups of rats (20 each) as needed to perform this test (1.209, 6.1). Test guideline 1.209, 7.5 states " This laboratory efficacy test should be replicated at least once." One more group of 20 animals should have been included to repeat the test. In this version of the test guidelines where the "single-feeding" claim is being pursued, a container must be switched to the other side of the cage with the opposite container after 12 hours (1.209,6.4) to show no preference to cage side or test dish type. No documentation is found to show that this was done.

The test results are summarized below:

Table 1. Wild Rats on Pelleted Bromethalin Bait

Pretest Weights **1-Day Test-Consumption and Mortality**

Sex	Average Group Weight (g)	OPP Diet Consumed (g)	Treated Bait Consumed (g)	Total Bait Consumption (g)
M (10)	285.4	18.1	156.6	174.7
F (10)	228.1	**100% Mortality**		Percent **Pelleted Bait** Consumed **89.6%**
Total (20)	Group Difference 57.3			

Table 2. Wild Rats on Control Bait

Pretest Weights **3-Day Test-Consumption and Mortality**

Sex	Average Group Weight (g)	OPP Diet Consumed (g)	Total Bait Consumption (g)
M (10)	294.6	362.7	362.7
F (10)	238.7	**0% Mortality**	
Total (20)	Group Difference 55.9		

3. **43689201C** Dickerson, C. W. November 24, 1992. Efficacy Testing of a Pelleted Rodenticide Bait Packaged in Place Packs. PM Resources, Inc. Unpublished Report. #62-893. 65pp.

DISCUSSION: Previous efficacy reviews for this product were conducted by W. Jacobs on October 10, 1995. In this efficacy review, W. Jacobs states to see other reviews in this jacket (67517-74) dated: "5/2/85, 10/4/90, 2/26/91 (which I did not find), 6/8/91, 9/15/95 (9/19/95), and 4/25/95..." for the background information for this product. ...This report (MRID # 43689201) describes an acceptable placepack-penetration study..." and "Mortality of 90% meets the mortality criterion for placepack-penetration studies run under laboratory conditions." (From page 15 of W. Jacobs review dated 10/10/95).

W. Jacobs stated in other reviews related to this product : "New efficacy data were submitted. These studies were assigned MRID Nos. 42025102 and 42025103. In her letter of 9/6/91, Kelly Kraft of Purina Mills states that "these studies are copies of tests submitted previously for 602-316 (67517-74) and assigned MRID Nos. 41591202 and 41591203. Those studies were discussed in the efficacy review of 10/4/90 for 602-316 (67517-74) and were accepted. The protocol (OPP guideline 1.219) used in this efficacy study was written in 1974, and was updated in 1991.

Wistar rat species were used for this study. The animals were weighed for the test October 26, 1992, and held pretest until November 2, 1992, which was 7 days before the test start. The guidelines specify (1.219, 3.1): "Subjects shall be healthy, active, sexually mature, and shall fall within the following weight classes in grams within seven days prior to start of the test: the rats should not have a maximum difference in average weights between the sexes of more than 65 g. The rats had a maximum acceptable difference in average pretest weights of 56.97 g before the testing.

Information on pages 52 to 56 of 65, describes the Standard Operating Procedure (SOP) under which these tests were run. The cage type and size, feeders and their

design, the pretest holding conditions, temperature, humidity and light conditions pretest, holding, and testing are described in this SOP, but were not documented very well in this study. The protocol that was developed for this study defines all of these parameters mentioned above and no deviations were noted. Information regarding the animal's water system was not explained (1.219, 7.3), These conditions may affect the outcome of the testing if they are extreme.

The composition and formulation of the OPP rat and mouse challenge diet (page 9 of 65) was well documented as well as the bait formulation, raw data (on page 2 of 5 in the Confidential attachment), and analysis (pages 26 to 51 of 65).

This test consisted of a minimum of two groups of rats (20 each) as needed to perform this test (1.219, 7.1). Test guideline 1.219, 8.5 states " This laboratory efficacy test should be replicated at least once." One more group of 20 animals should have been included to repeat this test at the same time. The guidelines state in 1.219, 8.1: "Maintain the test period for three days. If 100% mortality of bait exposed rats occurs prior to three days, monitoring of control group animals must continue for the 15 day test period plus the full follow up period." Mortality was 90%. There is no criterion in this guideline for palatability. Other guidelines prefer 33% treated bait consumption to show palatablilty. The treated bait consumption for this test was low: 15.9%.

The test results are summarized below:

Table 1. Wild Rats on Pelleted Bromethalin Bait

Pretest Weights **1-Day Test-Consumption and Mortality**

Sex	Average Group Weight (g)	OPP Diet Consumed (g)	Treated Bait Consumed (g)	Total Bait Consumption (g)
M (10)	202.8	1101.6	208.0	1309.6
F (10)	199.4	**90% Mortality**		Percent Pelleted Bait Consumed **15.9%**
Total (20)	Group Difference 3.4			

Table 2. Wild Rats on Control Bait

Pretest Weights **3-Day Test-Consumption and Mortality**

Sex	Average Group Weight (g)	OPP Diet Consumed (g)	Total Bait Consumption (g)
M (10)	202.5	4479.4	4479.4
F (10)	200.8	**0% Mortality**	
Total (20)	Group Difference		

	1.7	

4. **43859001C** Dickerson, C. W. August 24, 1995. Efficacy testing of a pelleted rodenticide bait, packaged in place packs and offered to laboratory rats. Vol 1. PM Resources, Inc. Unpublished Report. Experiment # 971. 41pp.

DISCUSSION: A previous efficacy review for this product was conducted by W. Jacobs on January 11, 1996. In this efficacy review, W. Jacobs states in his "Background Information" section to see other reviews in this jacket (67517-74) dated: "5/2/85, 9/15/85, 10/4/90, 2/26/91 (which I did not find), 6/8/91, 4/25/95, and 10/10/95." Other studies have been submitted to support the claims for this product. For example, in her letter of 9/6/91, Kelly Kraft of Purina Mills states that "these studies are copies of tests submitted previously for 602-316 (67517-74) and assigned MRID Nos. 41591202 and 41591203. Those studies were discussed in the efficacy review of 10/4/90 for 602-316 (67517-74) and were accepted. The protocol (OPP guideeline 1.219) used in this efficacy study was written in 1974, and was updated in 1991.

Wistar rat species were used for this study. The animals were weighed for the test June 19, 1995, and held pretest from June 19, 1995 to June 26, 1995 which was 7 days before the test start. The guidelines specify (1.219, 3.1): "Subjects shall be healthy, active, sexually mature, and shall fall within the following weight classes in grams within seven days prior to start of the test: the rats should not have a maximum difference in average weights between the sexes of more than 50 g. Animals shall be weighed no more than three days before the start of the bait exposure." The rats had a maximum acceptable difference in average pretest weights of 36.89 g seven days before the testing.

Information on pages 28 to 32 of 41, describes the Standard Operating Procedure (SOP) under which this test was run. The feeders and their design (1.219, 4.3) are not known what type of material they are made of and the watering apparatus was not described as "glass with ball-type watering tubes" (1.219, 7.3). No raw data is presented to show the pretest holding conditions, temperature, humidity and light conditions pretest, holding, and during testing are not mentioned in this SOP, and were not documented in this study. These conditions may affect the outcome of the testing if they are extreme. The guideline 1.219, 1.2 states: "Tests run according to this method must be supplemented by a test run according to OPP 1.209, Standard Norway Rat and Roof Rat Acute Dry Bait Laboratory Test Method, in which the toxic bait is remove from the package and tested separately." For this see MRID #'s 41591202 and 41591203.

The composition and formulation of the OPP rat and mouse challenge diet (page 10 and 16 of 41) was well documented as well as the bait formulation, raw data (on page 2 of 3 in the Confidential attachment), and analysis (pages 15 to 27 of 41).

This test consisted of a minimum of two groups of rats (20 each) as needed to perform this test (1.219, 7.1). Test guideline 1.219, 8.5 states " This laboratory efficacy test should be replicated at least once." One more group of 20 animals should have been included to repeat this test at the same time. The guidelines state in 1.219, 8.1: "Maintain the test period for three days. If 100% mortality of bait exposed rats occurs prior to three days, monitoring of control group animals must continue for the 15 day test period plus the full follow up period." The control animals were maintained for 15 days and the treated animals died after 1 to 4 days for males and 1 to 2 days for females. Other guidelines prefer 33% treated bait consumption to show palatablilty. The treated bait consumption for this test was low: 23.2%.

The test results are summarized below:

Table 1. Wild Rats on Pelleted Bromethalin Bait

Pretest Weights **1-Day Test-Consumption and Mortality**

Sex	Average Group Weight (g)	OPP Diet Consumed (g)	Treated Bait Consumed (g)	Total Bait Consumption (g)
M (10)	167.3	925.9	280.0	1205.9
F (10)	170.5	**100% Mortality**		Percent **Pelleted Bait** Consumed **23.2%**
Total (20)	Group Difference 3.2			

Table 2. Wild Rats on Control Bait

Pretest Weights **3-Day Test-Consumption and Mortality**

Sex	Average Group Weight (g)	OPP Diet Consumed (g)	Total Bait Consumption (g)
M (10)	168.5	3498.4	3498.4
F (10)	169.7	**0% Mortality**	
Total (20)	Group Difference 1.2		

5. **43859002C** Dickerson, C. W. August 24, 1995. Efficacy testing of a pelleted rodenticide bait, packaged in place packs and offered to laboratory rats. Vol 1. PM Resources, Inc. Unpublished Report. Experiment # 971. 41pp.

DISCUSSION: As stated previously, the efficacy review for this product was conducted by W. Jacobs on January 11, 1996. In this efficacy review, W. Jacobs states in his "Background Information" section to see other reviews in this jacket (67517-74)

dated: "5/2/85, 9/15/85, 10/4/90, 2/26/91 (which I did not find), 6/8/91, 4/25/95, and 10/10/95." Other studies have been submitted to support the claims for this product. For example, in her letter of 9/6/91, Kelly Kraft of Purina Mills states that "these studies are copies of tests submitted previously for 602-316 (67517-74) and assigned MRID Nos. 41591202 and 41591203. Those studies were discussed in the efficacy review of 10/4/90 for 602-316 (67517-74) and were accepted. The protocol (OPP guideeline 1.219) used in this efficacy study was written in 1974, and was updated in 1991.

Wistar rat species were used for this study. The animals were weighed for the test June 19, 1995, and held pretest from June 19, 1995 to June 26, 1995 which was 7 days before the test start. The guidelines specify (1.219, 3.1): "Subjects shall be healthy, active, sexually mature, and shall fall within the following weight classes in grams within seven days prior to start of the test: the rats should not have a maximum difference in average weights between the sexes of more than 50 g. Animals shall be weighed no more than three days before the start of the bait exposure." The rats had a maximum acceptable difference in average pretest weights of 32.89 g seven days before the testing.

Information on pages 28 to 32 of 41, describes the Standard Operating Procedure (SOP) under which this test was run. The feeders and their design (1.219, 4.3) are not known what type of material they are made of and the watering apparatus was not described as "glass with ball-type watering tubes" (1.219, 7.3). No raw data is presented to show the pretest holding conditions, temperature, humidity and light conditions pretest, holding, and during testing are not mentioned in this SOP, and were not documented in this study. These conditions may affect the outcome of the testing if they are extreme. The guideline 1.219, 1.2 states: "Tests run according to this method must be supplemented by a test run according to OPP 1.209, Standard Norway Rat and Roof Rat Acute Dry Bait Laboratory Test Method, in which the toxic bait is remove from the package and tested separately." For this see MRID #'s 41591202 and 41591203.

The composition and formulation of the OPP rat and mouse challenge diet (page 10 and 16 of 41) was well documented as well as the bait formulation, raw data (on page 2 of 3 in the Confidential attachment), and analysis (pages 15 to 27 of 41).

This test consisted of a minimum of two groups of rats (20 each) as needed to perform this test (1.219, 7.1). Test guideline 1.219, 8.5 states " This laboratory efficacy test should be replicated at least once." One more group of 20 animals should have been included to repeat this test at the same time. The guidelines state in 1.219, 8.1: "Maintain the test period for three days. If 100% mortality of bait exposed rats occurs prior to three days, monitoring of control group animals must continue for the 15 day test period plus the full follow up period." The control animals were maintained for 15 days and the treated animals died after 1 to 2 days for males and 1 to 2 days for females. Other guidelines prefer 33% treated bait consumption to show palatablilty. The treated bait consumption for

this test was very low: 0.07%.

The test results are summarized below:

Table 1. Wild Rats on Pelleted Bromethalin Bait
Pretest Weights 1-Day Test-Consumption and Mortality

Sex	Average Group Weight (g)	OPP Diet Consumed (g)	Treated Bait Consumed (g)	Total Bait Consumption (g)
M (10)	170.4	830.6	63.8	894.4
F (10)	174.5	**100% Mortality**		Percent **Pelleted Bait** Consumed **0.07%**
Total (20)	Group Difference 4.1			

Table 2. Wild Rats on Control Bait
Pretest Weights 3-Day Test-Consumption and Mortality

Sex	Average Group Weight (g)	OPP Diet Consumed (g)	Total Bait Consumption (g)
M (10)	168.5	3498.4	3498.4
F (10)	169.7	**0% Mortality**	
Total (20)	Group Difference 1.2		

6. **43859003C** Dickerson, C. W. August 24, 1995. Efficacy testing of a pelleted rodenticide bait, packaged in place packs and offered to laboratory rats. Vol 3. PM Resources, Inc. Unpublished Report. Experiment. 41pp. #62-973

DISCUSSION: As stated previously, the efficacy review for this product was conducted by W. Jacobs on January 11, 1996. In this efficacy review, W. Jacobs states in his "Background Information" section to see other reviews in this jacket (67517-74) dated: "5/2/85, 9/15/85, 10/4/90, 2/26/91 (which I did not find), 6/8/91, 4/25/95, and 10/10/95." Other studies have been submitted to support the claims for this product. For example, in her letter of 9/6/91, Kelly Kraft of Purina Mills states that "these studies are copies of tests submitted previously for 602-316 (67517-74) and assigned MRID Nos. 41591202 and 41591203. Those studies were discussed in the efficacy review of 10/4/90 for 602-316 (67517-74) and were accepted. The protocol (OPP guideeline 1.219) used in this efficacy study was written in 1974, and was updated in 1991.

Wistar rat species were used for this study. The animals were weighed for the test June 19, 1995, and held pretest from June 19, 1995 to June 26, 1995 which was 7 days before the test start. The guidelines specify (1.219, 3.1): "Subjects shall be healthy, active, sexually mature, and shall fall within the following weight classes in grams within seven days prior to start of the test: the rats should not have a maximum difference in average weights between the sexes of more than 50 g. Animals shall be weighed no more than three days before the start of the bait exposure." The rats had a maximum acceptable difference in average pretest weights of 30.38 g seven days before the testing.

Information on pages 28 to 32 of 41, describes the Standard Operating Procedure (SOP) under which this test was run. The feeders and their design (1.219, 4.3) are not known what type of material they are made of and the watering apparatus was not described as "glass with ball-type watering tubes" (1.219, 7.3). No raw data is presented to show the pretest holding conditions, temperature, humidity and light conditions pretest, holding, and during testing are not mentioned in this SOP, and were not documented in this study. These conditions may affect the outcome of the testing if they are extreme. The guideline 1.219, 1.2 states: "Tests run according to this method must be supplemented by a test run according to OPP 1.209, Standard Norway Rat and Roof Rat Acute Dry Bait Laboratory Test Method, in which the toxic bait is remove from the package and tested separately." For this see MRID #'s 41591202 and 41591203.

The composition and formulation of the OPP rat and mouse challenge diet (page 10 and 16 of 41) was well documented as well as the bait formulation, raw data (on page 2 of 3 in the Confidential attachment), and analysis (pages 15 to 27 of 41). The rats perforated all five packages in pen 3 and 3 packages were emptied in pen 5 (replaced). All five packages in pen 6 were perforated and 4 were emptied. The 4 packs were replaced, but none were perforated.

This test consisted of a minimum of two groups of rats (20 each) as needed to perform this test (1.219, 7.1). Test guideline 1.219, 8.5 states " This laboratory efficacy test should be replicated at least once." One more group of 20 animals should have been included to repeat this test at the same time. The guidelines state in 1.219, 8.1: "Maintain the test period for three days. If 100% mortality of bait exposed rats occurs prior to three days, monitoring of control group animals must continue for the 15 day test period plus the full follow up period." The control animals were maintained for 8 days and the treated animals died after 1 to 2 days for males and 1 to 2 days for females. Other guidelines prefer 33% treated bait consumption to show palatablilty. The treated bait consumption for this test was very low: 0.10%.

The test results are summarized below:

Table 1. Wild Rats on Bromethalin Placepack Bait

Pretest Weights 1-Day Test-Consumption and Mortality

Sex	Average Group Weight (g)	OPP Diet Consumed (g)	Treated Bait Consumed (g)	Total Bait Consumption (g)
M (10)	163.2	560.1	63.8	623.9
F (10)	170.8	**100% Mortality**		Percent Pelleted Bait Consumed **0.10%**
Total (20)	Group Difference 7.6			

Table 2. Wild Rats on Control Bait

Pretest Weights 3-Day Test-Consumption and Mortality

Sex	Average Group Weight (g)	OPP Diet Consumed (g)	Total Bait Consumption (g)
M (10)	168.5	3730.4	3730.4
F (10)	169.7	**0% Mortality**	
Total (20)	Group Difference 1.2		

7. **42025103C** Dickerson, C. W. June 21, 1990. Contains 0.01% Bromethalin Purina Last : N-Methyl 1-2, 4-Dinitro-N-(2, 4, 6-Tribromophenyl)-6-(Trifluoromethyl) Benzenamine. Purina Mills, Inc. Unpublished Report. Experiment. 43pp.#761

DISCUSSION: In the efficacy review by W. Jacobs (May 6, 1992), he states: "This product was registered without an efficacy review. This bait is claimed to be identical in formulation to PURINA ASSAULT RAT PLACE PACK BRAND (602-316) but is packaged in bulk ("loose bait") form and , as a result, has slightly different application directions on its label." In a later paragraph, W. Jacobs states "New efficacy data were submitted. These studies were assigned MRID Nos. 42025102 and 42025103. In her letter of 9/6/91, Kelly Kraft of Purina Mills states that these studies are copies of tests submitted previously for 602-316 and assigned MRID Nos. 41591202 and 41591203. Those studies were discussed in the efficacy review of 10/4/90 for 602-316 and were accepted. I have examined the report of efficacy studies submitted for 602-322 and have concluded that these reports refer

to the same studies that were submitted earlier for 602-316 and that were cited by Ms. Kraft. No /Additional efficacy studies are required for 602-322." The protocol (OPP guideeline 1.209) used in this efficacy study was written in 1974, and was updated in 1991.

The rats were wild-type captured and weighed April 30, 1990. They were weighed 7 days before the test start (May 7, 1990). The guidelines specify (1.209, 2.1) the rats should not have a maximum difference in average weights between the sexes of more than 65 g and they should not be weighed more than 3 days before the test. The 40 rats had a maximum acceptable difference in average weights of 12.10 g one week before the testing.

Information about the cage type and size, feeders and their design, and the pretest holding conditions were not available in the study documentation (1.209, 3 and 4). The temperature, humidity and light conditions pretest, holding, and testing were not documented as well (1.209, 5.1). Information regarding the animal's water system was not explained (1.209, 6.2), and how spillage was recaptured was not discussed (1.209, 6.3) . These conditions may affect the outcome of the testing if they are extreme.

The composition and formulation of the OPP rat and mouse challenge diet (page 11 of 42 and raw data on page 20 of 42) was well documented as well as the bait formulation (raw data page 19 of 42) and analysis (pages 23 to 30 of 42). The male and female control groups were used for MRID 41591202 (test #760) and 41591203 (test #761).

This test consisted of a minimum of two groups of rats (20 each) as needed to perform this test (1.209, 6.1). Test guideline 1.209, 7.5 states " This laboratory efficacy test should be replicated at least once." One more group of 20 animals should have been included to repeat the test. In this version of the test guidelines where the "single-feeding" claim is being pursued, a container must be switched to the other side of the cage with the opposite container after 12 hours (1.209,6.4) to show no preference to cage side or test dish type. No documentation is found to show that this was done.

The test results are summarized below:

Table 1. Wild Rats on Pelleted Bromethalin Bait

Pretest Weights **1-Day Test-Consumption and Mortality**

Sex	Average Group Weight (g)	OPP Diet Consumed (g)	Treated Bait Consumed (g)	Total Bait Consumption (g)
M (10)	285.4	18.1	156.6	174.7
F (10)	228.1	**100% Mortality**		Percent Pelleted Bait Consumed **89.6%**
Total (20)	Group Difference			

	57.3		

Table 2. Wild Rats on Control Bait

Pretest Weights **3-Day Test-Consumption and Mortality**

Sex	Average Group Weight (g)	OPP Diet Consumed (g)	Total Bait Consumption (g)
M (10)	294.6	784.4	784.4
F (10)	238.7	**0% Mortality**	
Total (20)	Group Difference 55.9		

8. **42025102C** Dickerson, C. W. June 21, 1990. Contains 0.01% Bromethalin Purina Last : N-Methyl 1-2, 4-Dinitro-N-(2, 4, 6-Tribromophenyl)-6-(Trifluoromethyl) Benzenamine. Purina Mills, Inc. Unpublished Report. Experiment. 43pp. #760.

DISCUSSION: In the efficacy review by W. Jacobs (May 6, 1992), he states: "This product was registered without an efficacy review. This bait is claimed to be identical in formulation to PURINA ASSAULT RAT PLACE PACK BRAND (602-316) but is packaged in bulk ("loose bait") form and , as a result, has slightly different application directions on its label." In a later paragraph, W. Jacobs states "New efficacy data were submitted. These studies were assigned MRID Nos. 42025102 and 42025103. In her letter of 9/6/91, Kelly Kraft of Purina Mills states that these studies are copies of tests submitted previously for 602-316 and assigned MRID Nos. 41591202 and 41591203. Those studies were discussed in the efficacy review of 10/4/90 for 602-316 and were accepted. I have examined the report of efficacy studies submitted for 602-322 and have concluded that these reports refer to the same studies that were submitted earlier for 602-316 and that were cited by Ms. Kraft. No /Additional efficacy studies are required for 602-322." The protocol (OPP guideeline 1.209) used in this efficacy study was written in 1974, and was updated in 1991.

The rats were wild-type captured and weighed April 30, 1990. They were weighed 7 days before the test start (May 7, 1990). The guidelines specify (1.209, 2.1) the rats should not have a maximum difference in average weights between the sexes of more than 65 g and they should not be weighed more than 3 days before the test. The 40 rats had a maximum acceptable difference in average

weights of 28.6 g one week before the testing.

The rats were wild-type captured and weighed April 30, 1990. They were weighed 7 days before the test start. The guidelines specify (1.209, 2.1) the rats should not have a maximum difference in average weights between the sexes of more than 65 g and they should not be weighed more than 3 days before the test. The rats had a maximum acceptable difference in average weights of 28.6 g one week before the testing.

Information about the cage type and size, feeders and their design, and the pretest holding conditions were not available in the study documentation (1.209, 3 and 4). The temperature, humidity and light conditions pretest, holding, and testing were not documented as well (1.209, 5.1). Information regarding the animal's water system was not explained (1.209, 6.2), and how spillage was recaptured was not discussed (1.209, 6.3) . These conditions may affect the outcome of the testing if they are extreme.

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This test consisted of a minimum of two groups of rats (20 each) as needed to perform this test (1.209, 6.1). Test guideline 1.209, 7.5 states " This laboratory efficacy test should be replicated at least once." One more group of 20 animals should have been included to repeat the test. In this version of the test guidelines where the "single-feeding" claim is being pursued, a container must be switched to the other side of the cage with the opposite container after 12 hours (1.209,6.4) to show no preference to cage side or test dish type. No documentation is found to show that this was done.

The test results are summarized below:

Table 1. Wild Rats on Pelleted Bromethalin Bait

Pretest Weights **1-Day Test-Consumption and Mortality**

Sex	Average Group Weight (g)	OPP Diet Consumed (g)	Treated Bait Consumed (g)	Total Bait Consumption (g)
M (10)	315.2	35.8	146.1	181.9
F (10)	289.1	**100% Mortality**		Percent Pelleted Bait Consumed **80.3%**
Total (20)	Group Difference 26.1			

Table 2. Wild Rats on Control Bait

Pretest Weights **3-Day Test-Consumption and Mortality**

Sex	Average Group Weight (g)	OPP Diet Consumed (g)	Total Bait Consumption (g)
M (10)	294.6	810.2	810.2
F (10)	238.7	**0% Mortality**	
Total (20)	Group Difference 55.9		

Efficacy Comments

1. The rats needed to have an acceptable difference in average weights three days before testing. These rats were all weighed one week before the testing. This should be corrected in future tests.

2. The cage type and size, the feeders and their design, the temperature, humidity and light conditions, and the animal's water system are all critical to the repeatability of a test. The SOP's for these procedures were not provided with the document so I could not check to see if the guidelines were followed for these specifics. These conditions could affect the outcome of the testing if they were extreme. SOP's should be included when they are referenced in a study in any future submissions.

3. All of the studies were done with the minimum of animals without repeating the test. As called for in the guidelines, one more group of animals should have been used to verify the results. The additional test results must be submitted in future study submissions.

Conclusion(s): W. Jacobs is quoted in his January 11, 1996 review of three of the above studies: It is not clear that testing rats "...confined in a rather small and simple environment reflects the range of what might be expected from wild-type Norways under conditions of actual problematic rodent infestations. What the results of the test show is that the bait is toxic to rats..." With the omission of basic test information, a complete picture of the testing cannot be verified; however, I agree the W. Jacobs conclusions from his May 6th, 1992, review that "The efficacy data submitted to support the claims made for this product are acceptable."